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Description

The present invention relates to the preparation of chlorosucrose sweeteners and particularly to the preparation of such sweeteners in a stable form useful for incorporation in a variety of food and confectionery products as well as for medicinal uses, and to such stabilized sucralose compositions.

The sweetening agent known as sucralose comprises a chlorosucrose sweetener derived from a class of compounds based upon sucrose and galactosucrose in which one or more hydroxy groups are replaced by chlorine atoms, and is described in U.K. Patent No. 1,543,167. Of particular interest is the compound sucralose, (4-chloro-4-deoxy-α-D-galactopyranosyl 1,6-dichloro-1,6-dideoxy-β-D-fructofuranoside, also known as 4,1',6'-trichloro-4,1',6'-trideoxygalactosucrose). Sucralose and the other members of its chemical family have been identified as intensely sweet, offering a sweetness several hundred times that of sucrose, and are of particular interest for use as low calorie sweeteners to replace saccharin in various products, including foods, candy, comestibles, beverages and orally received medicinals such as cough drops.

This class of compounds is generally relatively stable and inert and particularly exhibits the stability in acid aqueous solutions, in marked contrast to peptide-based sweeteners such as aspartame. Under completely dry conditions, however, sucralose which is present in a crystalline form tends to discolour in response to elevated temperatures. For example, such discolouration can be exhibited after twenty minutes of exposure of pure dry sucralose to a temperature of 100 °C, wherein the colour changes to a pale brown.

Efforts have previously been undertaken to stabilize sucralose by various techniques. For example, in U.K. Patent Application No. 2,169,601A, sucralose is treated by co-crystallization with a nitrogenous base and in particular compounds containing an amine group such as niacinamide or an amino acid. An alternative approach was pursued by Jackson and Jenner and disclosed in European Patent Publication No. 0,255,260, wherein crystalline sucralose was prepared and then reduced to particles of critical dimension, in particular such particles no greater than 10 micrometres (microns) in mean particle size with a maximum particle size no greater than twice the mean.

Neither of the foregoing approaches has been totally satisfactory as the resulting sucralose products have continued to exhibit commercially undesirable thermal instability, and in the instance of the co-crystallization with the nitrogenous base material are further qualified in their acceptability by the admixture with a material that may be of reduced sweetness sensation.

A need therefore exists to develop a truly thermally stable form of sucralose that likewise maximizes the delivery of the sweetness sensation when such material is incorporated into foods and related comestible products.

According to the present invention there is provided a thermally stabilized sucralose composition comprising a co-crystallized complex of sucralose and at least 5% by weight of a cyclodextrin.

In accordance with the present invention, a thermally stabilized composition is prepared which comprises a co-crystallized complex of sucralose and a cyclodextrin, preferably β-cyclodextrin (β-CD). The co-crystallized complex comprises at least about 5% by weight of cyclodextrin and is prepared in particulate form to a uniform particle size. In a preferred embodiment, the co-crystallized complex comprises at least about 15% by weight of the cyclodextrin.

The complex may be prepared by dissolving a mixture of cyclodextrin and sucralose in a non-aqueous solvent such as methanol, followed by the removal of the methanol and the placement of the remaining slurry in a solvent such as ethyl acetate, filtering out the formed precipitate, washing the same with a further quantity of ethyl acetate and then drying the resulting crystals. Thereafter, the crystals may be ground down to the desired particle size and are ready for use.

The resulting crystalline complex exhibits extended thermal stability and can be incorporated into a variety of food, confectionery and medicinal products where sweeteners such as saccharin may be desirable. Accordingly, the present invention extends to such products having the complex included therein as an ingredient, such as anti-bacterial oral preparations and the like.

Accordingly, it is a principal object of the present invention to prepare a thermally stable form of the sweetener sucralose.

It is a still further object of the present invention to prepare the sweetener sucralose as aforesaid which exhibits extended thermal stability in conjunction with sweetness delivery comparable to that of the unmodified sweetener material.

It is a still further object of the present invention to provide a method for the preparation of a thermally stable complex of the sweetener sucralose which is simple and economical to perform.

It is a still further object of the present invention to prepare one or more comestible products containing a thermally stabilized complex including the sweetener sucralose.

It is a still further object of the present invention to prepare one or more food products containing a thermally stabilized complex of the sweetener sucralose.

It is a still further object of the present invention to prepare one or more medicinal products containing a thermally stabilized complex of the sweetener sucralose.

Other objects and advantages will become apparent to those skilled in the art from a review of the ensuring detailed description which proceeds with reference to the following illustrative drawings.

FIGURE 1 is a graph depicting the improvement in resistance to browning of the co-crystalline complex of the present invention over pure sucralose.

FIGURE 2 is a graph presenting the results of comparative testing of the sweetness intensity of chewing gums embodying the complex of the present invention with gums employing commercially available forms of sucralose.

As noted earlier, the present invention relates to preparation of the sweetener sucralose in a thermally stable form by the formation of a crystalline complex between sucralose and a cyclodextrin. More particularly, the complex constitutes a co-precipitate of the cyclodextrin and sucralose, with the cyclodextrin present in an amount of at least about 5% by weight, and more preferably at least about 15% by weight. The complex may be recovered and the resulting crystals may be comminuted to a uniform particle size.

The cyclodextrin used in the present invention (hereinafter abbreviated as CD) is a cyclic non-reducing oligosaccharide homolog formula of $(C_6H_{10}O_5)_n$, joined by α-1,4-glucosidic linkages to form a cyclic structure. Generally, 6 to 10 D-glucopyranose groups are bonded in this fashion, and form a rigid "doughnut-shaped" conical structure with a hollow interior of a specified volume. The resulting material is accordingly named α-CD, β-CD or τ-CD according to the degree of polymerization, i.e, 6, 7 or 8 glucose units. The interior of the ring contains C-H bonds or ether bonds and is thereby hydrophobic, while the exterior of the ring defines OH groups and is thereby hydrophilic. Because of its structure CD is able to entrap various compounds in its cyclic interior, and has recognized utility as a "molecular" encapsulant. For example, a variety of materials including aromatics, alcohols, halides and hydrogen halides, fatty acids and their esters are among the compounds that may be held within the internal cavity of cyclodextrin. The "guest" molecules must satisfy the size criterion of fitting at least partially into the cyclodextrin internal cavity, resulting in an inclusion complex.

CD has been used previously with foods to mask unwanted aromas, to prevent oxidation, to preserve flavours and to prevent moisture absorption, such as in sugared foods. CD has also found utility as a malodourous breath reducing agent, as as a stabilizer and bitterness reducer for citrus fruit and flavours.

The use of cyclodextrins in the functions indicated above is documented in the literature and, by way of example, attention is directed to Szejtli, J., "Cyclodextrins: A New Group of Industrial Basic Materials", DIE NAHRUNG, 29:9, 911-924 (1985); Nagamoto, S., "Cyclodextrins: Expanding the Development of Their Functions And Applications, CHEMICAL ECONOMY AND ENGINEERING REVIEW, Vol. 17, No. 7-8 (No. 190) pp. 28-35 (July/August 1985); U.S. Patent No. 4,267,166, U.S. Patent No. 4,332,825, U.S. Patent No. 4,751,095, and lastly, European Patent Application, Publication No. 097,950 in the name of Ajinomoto Co., Inc. The first two articles deal generally with the structure and utility of cyclodextrins, and disclose the broad scope of its utility. U.S. Patent No. 4,267,166 discloses the use of cyclodextrin as a foul breath preventive agent, while U.S. Patent No. 4,332,825, Nagamoto Supra. and Konno, A., et al., "Bitterness Reduction of Citrus Fruits by β-Cyclodextrin", AGRIC. BIOL. CHEM., 45 (10): 2341-2342 (1981), disclose the ability of cyclodextrin to reduce the bitterness of citrus by forming inclusion complexes with bitter compounds such as naringin and limonin. Finally, U.S. Patent No. 4,751,095 and the European Publication deal with the preparation of cyclodextrin complexes with aspartame. The last mentioned publications disclose the formation of stabilized inclusion complexes between the cyclodextrin and aspartame by the reaction of both materials in a common solvent, followed by drying of the formed complex, such drying being optional in the case of the European Publication. Both publications are distinguishable from the present invention in view of the obvious structural distinctions that exist between aspartame and sucralose and more particularly, the manner in which the complexes of the present invention are prepared.

CD is usually produced from starch by treating it with an amylase or similar enzyme produced from Bacillus macerans or an alkali-resistant bacterium. Although there are no particular limitations on the CD that can be used in the present invention, one can choose the particular CD, i.e. α-CD, β-CD or τ-CD depending upon the solubility of the resulting complex that one wishes to achieve. The respective cyclodextrins may be employed as a mixture in some instances, or when the use of a particular cyclodextrin is not critical. In the instance where the present complex is to be used as a food additive, β-CD is preferred.

As noted earlier, the co-crystallized complex of sucralose and cyclodextrin may be prepared simply by the formation of a solution of both ingredients in a non-aqueous solvent such as methanol, the removal of

the solvent and the placement of the resulting slurry in a solution with ethyl acetate, all of which may be conducted at room temperature. The ingredients may be added and retained therein for a period of time sufficient to permit co-crystallization to take place. Naturally, the temperature of the solution should not be unduly raised as discoloration of the sucralose component could occur.

More particularly, the inventive method comprises:

a) dissolving a quantity of sucralose and a stoichiometrically sufficient amount of a cyclodextrin in a suitable non-aqueous solvent;

b) maintaining the solution formed in step a) for a period of time sufficient to permit full co-crystallization of said sucralose and said cyclodextrin to take place;

c) recovering the crystalline reaction product from step b) and drying the same; and

d) subjecting the material from step c) to comminution to form particles therefrom.

The solution may be optionally subjected to stirring and may likewise be reduced in temperature and maintained under such conditions for a period of hours to allow crystallization to take place. Upon completion of crystal formation, the reaction product may be recovered such as by filtration, optionally washed with a further quantity of solvent, eg. ethyl acetate, and then dried. After drying is complete, the resulting crystals may be comminuted to uniform particle sizes, and thereafter transferred for storage or incorporation into various products.

The complexes prepared in accordance with the present invention are suitable for use in any aqueous food to replace sugars normally used as sweeteners. The term "aqueous foods" as used herein refers to all foods except dried foods and oily foods, and by way of non-limiting example, includes beverages such as fruit juices, such as citrus juices, vegetable juices such as tomato juice, cola, sports drinks (i.e. isotonically balanced drinks), coffee, tea, cocoa, dairy milk and milk-containing drinks, ginger ale; yogurt, jelly, puddings and mousse; sauces such as ketchup, mayonnaise, salad dressings, fruit-flavoured sauce, chocolate sauce, tomato sauce and chili sauce; creams, toppings, fillings and jams; frozen desserts such as ice creams and sherbets; pickle syrups, and pickling syrup; chewing gum, hard candies, nougat candies, jelly beans and the like.

In the instance where the complex of the present invention is to be incorporated in a chewing gum, the gum base may be any chewable, substantially water-insoluble base such as chicle or substitutes thereof, guttagkay, sorva, jelutong, synthetic resins, rubbers and the like and mixtures of these materials. The amount of gum base employed in the chewing gum may vary depending upon the particular base utilized and the other ingredients that make up the final product. Generally, however, the gum base may vary in amount from 15 to 40% by weight of the final composition, and preferably from 20 to 30% by weight.

Plasticizers or softeners such as lanolin, propylene, glycol, glycerol and the like and mixtures of these may optionally be incorporated within the gum base to achieve desired texture and consistency. The flavours employed in chewing gums may be the essential oils or synthetic flavours or mixtures of these. Flavours such as cinnamon, wintergreen, spearmint, peppermint, birch, anise, fruit flavours and the like may be utilized satisfactorily. The amount of flavouring is a matter of preference, but may be subject to such factors as the type of flavour and the type of base utilized in conjunction therewith. Generally, flavouring materials account for about 1% by weight of the total gum composition.

As it is generally desirable that the chewing gum possess a distinct and favourable sweetness, the remaining portion of the chewing gum is generally composed of water soluble carbohydrates, particularly bulk sweeteners such as sugar or sugar alcohols. Thus, in addition to the incorporation of the inventive co-crystallized complex of sucralose and CD, various sweeteners well-known in the art for their bulking and/or sweetening ability. For example, sugared chewing gum compositions may include sucrose, dextrose, corn syrup, galactose, glucose, fructose and substitutes, and mixtures thereof. Sugar substitutes may include any sweetening agents utilized in sugarless gum such as mannitol, sorbitol, xylitol, acid saccharin and its salts, cyclamates, and dipeptides such as aspartame, dihydrochalcone, glycyrrhizin, and Stevia rebaudiana - (Stevioside). Also contemplated as an additional sweetener is the non-fermentable sugar substitute (hydrogenated starch hydrolysate) which is described in U.S. Reissue Patent 26,959, and the synthetic sweetener 3,4-dihydro-6-methyl-1,2,3-oxathiazin-4-one-2,2-dioxide (acesulfame-K) particularly the potassium, sodium and calcium salts thereof as described in German Patent No. 2,001,017.7.

In the instance where the sucralose complex of the present invention is to be incorporated in a chewing gum, it may be utilized in an amount ranging from 0.02 to 0.25%, and will offer satisfactory sweetness. Naturally, the exact amount of sucralose complex incorporated in a given chewing gum may vary depending upon the desired sweetness level.

In addition, the complexes of the present invention can be incorporated into aqueous or aqueous-alcohol oral preparations such as mouthwashes, sprays, rinses, tooth pastes, dental creams or tooth powders. In such event, the complex should be present in amounts ranging 0.01% to 40% by weight and

more preferably, from 5% to 40% by weight of the final composition.

Oral preparations to which the inventive complex may be added can take a variety of textural forms. For example, in the case of dental creams, tooth pastes or tooth powders, the texture may be grainy or pasty. Likewise, gel-like preparations may be formulated utilizing agents such as colloidal silica and alkali metal alumino silicates.

As indicated with respect to chewing gums, the stabilized sucralose complex of the present invention is preferably used in conjunction with known natural and artificial sweeteners such as sucrose, saccharides, saccharin, acesulfame-K, aspartame and the like.

The present invention will now be better understood by reference to certain specific examples which are presented hereinafter for purposes of illustration and not limitation. In the examples, all percentages and parts as given, are expressed by weight unless otherwise stated.

EXAMPLE I

Several stabilized sucralose compositions were prepared by the following procedure. A quantity of β-cyclodextrin was added to sucralose and the resulting mixture was then dissolved in 25 ml. methanol and thereafter heated to 40 °C with the application of vacuum suction to draw off the methanol. After 1 hour the remaining slurry was dissolved in ethyl acetate and the resulting solution was heated to complete the formation of the solution. The solution was then cooled to 20 °C and allowed to crystallize overnight in a refrigerator. The crystalline precipitate was then filtered off by cold-filtration, and thereafter air-dried and then milled to a uniform particle size.

A series of samples of co-crystalline complexes were prepared for testing, and accordingly 0.25, 0.5 and 1.0 g of cyclodextrin were added to sucralose to prepare a total of 5 g of mixture. The samples thus corresponded to mixtures containing 5%, 10% and 20% cyclodextrin. As a comparison, a sample containing pure sucralose was prepared in the same manner, and was likewise milled identically to eliminate any particle size differences.

The powders thus prepared were subjected to a temperature of about 195 °F (92 °C) and were monitored during heating to note the length of time that it took for the respective samples to turn light brown and to thereby discolour. The results are set forth in Table 1, below.

TABLE 1

SAMPLE	ELAPSED TIME BEFORE DISCOLOURATION
SUCRALOSE ALONE	60 Minutes
SUCRALOSE-5% CYCLODEXTRIN	80 Minutes
SUCRALOSE-10% CYCLODEXTRIN	90 Minutes
SUCRALOSE-20% CYCLODEXTRIN	180 Minutes

Referring to Table 1, it is apparent that a 33.3% improvement in thermal stability as reflected in resistance to discolouration is achieved by the co-crystallization of sucralose with as little as 5% cyclodextrin, with a 50% improvement results from the use of 10% cyclodextrin. The most dramatic improvement of 300% was seen when co-crystallization was conducted with 20% by weight of cyclodextrin. A complex containing only 1% cyclodextrin was also prepared and tested, and although the data was not presented above, it indicated that such a minimal concentration of cyclodextrin was largely ineffective.

Lastly, it was noted that the measurements and results presented herein were more apparent when the tests were conducted at the lower temperature range selected.

EXAMPLE II

Additional thermal stability testing was conducted between a free sucralose control and samples containing 2%, 3%, 5%, 10% and 15% cyclodextrin, respectively, for the purpose of confirming the results of the tests conducted in Example 1, and to determine the activity and effectiveness of inventive complexes prepared with other variant cyclodextrin contents. The preparation of the control and inventive samples was the same as that employed with the samples of Example 1. The temperature applied during the stability test was 90 °C ± 3 °C (195 °F ± 5 °F). The results are set forth in Table 2 below, as well as in Figure 1, which represents a plot of time delay in discolouration of the inventive samples over the control samples of pure sucralose and 2% and 3% cyclodextrin.

TABLE 2

SAMPLE	ELAPSED TIME BEFORE DISCOLORATION	MINUTES DELAYED VS. FREE SUCRALOSE
SUCRALOSE ALONE	65 Minutes	0
SUCRALOSE-2% CYCLODEXTRIN	69 Minutes	4
SUCRALOSE-3% CYCLODEXTRIN	72 Minutes	7
SUCRALOSE-5% CYCLODEXTRIN	82 Minutes	17
SUCRALOSE-10% CYCLODEXTRIN	94 Minutes	29
SUCRALOSE-15% CYCLODEXTRIN	136 Minutes	71

The data presented above and in Figure 1 further confirm the threshold of significant thermal stability exhibited by the use of 5% cyclodextrin, and also demonstrates a substantial improvement in stability as the level of cyclodextrin is increased from 10% to 15%.

EXAMPLE III

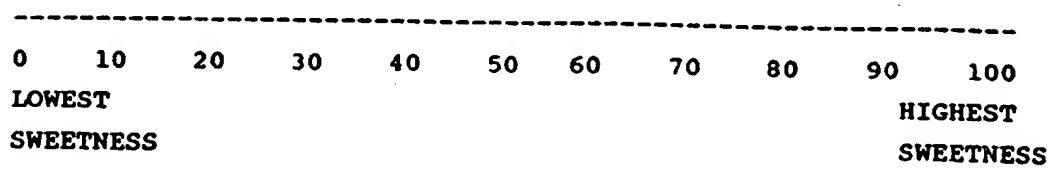
In this Example, a comparison was made between complexes of the present invention that differed as to the quantity of cyclodextrin present, to determine whether the presence of cyclodextrin has any effect on the sweetness intensity and delivery of the sucralose component. Accordingly, 0.29 g of a complex containing 5% cyclodextrin and 0.31 g of a complex containing 10% cyclodextrin were separately dissolved in 100 g of water to form equivalent solutions of 0.28% sucralose content. A solution containing 0.28% of free sucralose was also prepared and tested.

Equal samples of each of the solutions were given to an expert panel. The panel concluded that all of the solutions were sweet and noted no differences among the respective solutions. From the above results, it can be concluded that cyclodextrin in these amounts does not diminish the sweetness delivery and sensation offered by sucralose.

EXAMPLE IV

The sweetness intensity of the invention in a gum formulation was compared herein with that of free sucralose, a co-crystalline complex of sucralose and niacinamide, the latter prepared in accordance with the procedures taught in the United Kingdom Application No. 2,169,601A to Jackson, disclosed earlier herein. Specifically, samples of the inventive complex containing 5% cyclodextrin, free sucralose and the complex of Jackson publication prepared with 3% by weight of niacinamide, were respectively formulated and incorporated into otherwise identical spearmint flavoured chewing gums in equal amounts and by equally identical procedures. After formulation, the gum samples were subjected to expert chew panel evaluation of sweetness intensity.

Accordingly, the gum samples were given to a panel of scientists, all of whom chew on a regular basis for the purpose of screening the samples. During the experiment each panelist was asked to evaluate the sweetness intensity of each of the samples and to render an opinion based on the following numerical values.



The panelists were asked to rate the samples at intervals of 30 seconds, 2 minutes and 6 minutes. The results of the ratings assigned by each of the panelists to each of the samples were averaged together and then compared. The data are expressed in graphical form in Figure 2.

As can be seen from Figure 2, the sample containing the inventive sucralose complex was rated better as to sweetness than both of the other samples. Acccordingly, the present complex offered an initial sweetness that was greater than free sucralose. By comparison, the sample prepared in accordance with

the Jackson disclosure offered the lowest initial sweetness intensity.

The present disclosure is to be considered as in all respects illustrative and not restrictive, the scope of the invention being indicated by the appended Claims.

Claims

Claims for the following Contracting States : BE, FR, DE, IT, NL, LI, SE, CH, GB

1. A thermally stabilized sucralose composition comprising a co-crystallized complex of sucralose and at least 5% by weight of a cyclodextrin.

2. A composition according to claim 1, wherein the cyclodextrin is α-cyclodextrin, β-cyclodextrin, γ-cyclodextrin or mixtures thereof.

3. A composition according to claim 1 or 2, wherein the sucralose is at least partially entrapped within the cyclodextrin.

4. A composition according to claim 1, 2 or 3, wherein the complex contains at least 15% by weight of the cyclodextrin.

5. A composition according to any preceding claim, wherein the complex is in particulate form.

6. A composition according to claim 5, wherein the average particle size in the complex is approximately 10 micrometres.

7. A process for the preparation of a thermally stabilized sucralose composition according to any one of claims 1 to 6, which process comprises:
   (a) dissolving sucralose and a cyclodextrin in a suitable non-aqueous solvent;
   (b) maintaining the solution formed in step (a) for a period of time sufficient to permit full co-crystallization of the sucralose and cyclodextrin to take place;
   (c) recovering then drying the crystalline reaction product from step (b); and
   (d) comminuting the material from step (c) into particulate form.

8. A method according to claim 7, wherein the non-aqueous solvent is methanol or ethyl acetate, or both.

9. A method according to claim 7 or 8, wherein the solution is maintained in step (b) for up to eight hours.

10. An orally ingestible product containing a sweetener, wherein the sweetener comprises a composition according to any one of claims 1 to 6, wherein the ingestible product is a: solid or aqueous food; liquid beverage; chewing gum composition; mouth wash; cough sweet; breath freshener; or confectionery product such as a hard or soft candy, chocolate or biscuit.

11. An orally ingestible pharmaceutical preparation containing a sweetener which comprises a composition according to any one of claims 1 to 6.

Claims for the following Contracting State : GR

1. A thermally stabilized sucralose composition comprising a co-crystallized complex of sucralose and at least 5% by weight of a cyclodextrin.

2. A composition according to claim 1, wherein the cyclodextrin is α-cyclodextrin, β-cyclodextrin, γ-cyclodextrin or mixtures thereof.

3. A composition according to claim 1 or 2, wherein the sucralose is at least partially entrapped within the cyclodextrin.

4. A composition according to claim 1, 2 or 3, wherein the complex contains at least 15% by weight of the cyclodextrin.

5. A composition according to any preceding claim, wherein the complex is in particulate form.

6. A composition according to claim 5, wherein the average particle size in the complex is approximately 10 micrometres.

7. A process for the preparation of a thermally stabilized sucralose composition according to any one of claims 1 to 6, which process comprises:
(a) dissolving sucralose and a cyclodextrin in a suitable non-aqueous solvent;
(b) maintaining the solution formed in step (a) for a period of time sufficient to permit full co-crystallization of the sucralose and cyclodextrin to take place;
(c) recovering then drying the crystalline reaction product from step (b); and
(d) comminuting the material from step (c) into particulate form.

8. A method according to claim 7, wherein the non-aqueous solvent is methanol or ethyl acetate, or both.

9. A method according to claim 7 or 8, wherein the solution is maintained in step (b) for up to eight hours.

10. An orally ingestible product containing a sweetener, wherein the sweetener comprises a composition according to any one of claims 1 to 6, wherein the ingestible product is a: solid or aqueous food; liquid beverage; chewing gum composition; mouth wash; cough sweet; breath freshener; or confectionery product such as a hard or soft candy, chocolate or biscuit.

11. A process for the preparation of an orally ingestible pharmaceutical preparation which comprises incorporating into a pharmaceutical preparation a sweetener comprising a stabilized composition according to any one of claims 1 to 6.

Claims for the following Contracting State : ES

1. A process for the preparation of a thermally stabilized sucralose composition comprising a co-crystallized complex of sucralose and at least 5% by weight of a cyclodextrin which process comprises the steps of:
(a) dissolving the sucralose and cyclodextrin in a suitable non-aqueous solvent; and
(b) maintaining the solution formed in step (a) for a period of time sufficient to permit full co-crystallization of the sucralose and cyclodextrin to take place;
(c) recovering and then drying the crystalline reaction product from step (b); and
(d) comminuting the material from step (c) to particulate form.

2. A process according to claim 1, wherein the cyclodextrin is α-cyclodextrin, β-cyclodextrin, γ-cyclodextrin or mixtures thereof.

3. A process according to claim 1 or 2, wherein the sucralose is at least partially entrapped within the cyclodextrin.

4. A process according to any preceding claim, wherein the complex contains at least 15% by weight of the cyclodextrin.

5. A process according to any preceding claim, wherein in step (d) the material is comminuted to an average particle size of approximately 10 micrometres.

6. A process according to any preceding claim, wherein the non-aqueous solvent is methanol or ethyl acetate, or both.

7. A process according to any preceding claim, wherein the solution is maintained in step (b) for up to eight hours.

8. A process for the preparation of an orally ingestible product, which comprises incorporating into a product an orally ingestible product containing a sweetener, wherein the sweetener comprises a composition prepared by a process according to any one of claims 1 to 7, wherein the ingestible

product is a: solid or aqueous food; liquid beverage; chewing gum composition; mouth wash; cough sweet; breath freshener; or confectionery product such as a hard or soft candy, chocolate or biscuit.

9. A process for the preparation of an orally ingestible pharmaceutical preparation which comprises incorporating into a pharmaceutical preparation a sweetener comprising a stabilized composition prepared by a process according to any one of claims 1 to 7.

Patentansprüche

Patentansprüche für folgende Vertragsstaaten : BE, FR, DE, IT, NL, LI, SE, CH, GB

1. Wärmestabilisierte Sucralosemasse, umfassend einen gemeinsam kristallisierten Komplex aus Sucralose und mindestens 5 Gew.-% eines Cyclodextrins.

2. Masse nach Anspruch 1, wobei das Cyclodextrin aus α-Cyclodextrin, β-Cyclodextrin, γ-Cyclodextrin oder Mischungen derselben besteht.

3. Masse nach Anspruch 1 oder 2, wobei die Sucralose zumindest teilweise innerhalb des Cyclodextrins eingeschlossen ist.

4. Masse nach Anspruch 1, 2 oder 3, wobei der Komplex mindestens 15 Gew. -% des Cyclodextrins enthält.

5. Masse nach einem der vorhergehenden Ansprüche, wobei der Komplex in teilchenförmiger Form vorliegt.

6. Masse nach Anspruch 5, wobei die durchschnittliche Teilchengröße im Komplex etwa 10µm beträgt.

7. Verfahren zur Herstellung einer wärmestabilisierten Sucralosemasse nach einem der Ansprüche 1 bis 6, durch
   (a) Auflösen von Sucralose und eines Cyclodextrins in einem geeignetem nicht-wässrigen Lösungsmittel;
   (b) ausreichend langes Stehenlassen der in Stufe (a) gebildeten Lösung zur vollständigen gemeinsamen Kristallisation der Sucralose und des Cyclodextrins;
   (c) Gewinnen und anschließendes Trocknen des kristallinen Reaktionsprodukts aus Stufe (b) und
   (d) Vermahlen des Materials aus Stufe (c) zu Teilchenform.

8. Verfahren nach Anspruch 7, wobei das nicht-wässrige Lösungsmittel aus Methanol und/oder Ethylacetat besteht.

9. Verfahren nach Anspruch 7 oder 8, wobei die Lösung in Stufe (b) bis zu 8h lang stehen gelassen wird.

10. Oral einnehmbares Produkt mit einem eine Masse nach einem der Ansprüche 1 bis 6 umfassenden Süßungsmittel, wobei das einnehmbare Produkt aus einem festen oder wässrigen Nahrungsmittel, einem flüssigen Getränk, einer Kaugummimasse, einem Mundwasser, einem Hustenbonbon, einem Atemfrischmacher oder einem Süßwaren- oder Zuckerwerkprodukt, z.B. Bonbons oder weichem Zukkerwerk, Schokolade oder Bisquit besteht.

11. Oral einnehmbare Arzneimittelzubereitung mit einem Süßungsmittel, umfassend eine Masse nach einem der Ansprüche 1 bis 6.

Patentansprüche für folgenden Vertragsstaat : GR

1. Wärmestabilisierte Sucralosemasse, umfassend einen gemeinsam kristallisierten Komplex aus Sucralose und mindestens 5 Gew. -% eines Cyclodextrins.

2. Masse nach Anspruch 1, wobei das Cyclodextrin aus α-Cyclodextrin, β-Cyclodextrin, γ-Cyclodextrin oder Mischungen derselben besteht.

3. Masse nach Anspruch 1 oder 2, wobei die Sucralose zumindest teilweise innerhalb des Cyclodextrins eingeschlossen ist.

4. Masse nach Anspruch 1, 2 oder 3, wobei der Komplex mindestens 15 Gew. -% des Cyclodextrins enthält.

5. Masse nach einem der vorhergehenden Ansprüche, wobei der Komplex in teilchenförmiger Form vorliegt.

6. Masse nach Anspruch 5, wobei die durchschnittliche Teilchengröße im Komplex etwa 10µm beträgt.

7. Verfahren zur Herstellung einer wärmestabilisierten Sucralosemasse nach einem der Ansprüche 1 bis 6, durch
   (a) Auflösen von Sucralose und eines Cyclodextrins in einem geeignetem nicht-wässrigen Lösungsmittel;
   (b) ausreichend langes Stehenlassen der in Stufe (a) gebildeten Lösung zur vollständigen gemeinsamen Kristallisation der Sucralose und des Cyclodextrins;
   (c) Gewinnen und anschließendes Trocknen des kristallinen Reaktionsprodukts aus Stufe (b) und
   (d) Vermahlen des Materials aus Stufe (c) zu Teilchenform.

8. Verfahren nach Anspruch 7, wobei das nicht-wässrige Lösungsmittel aus Methanol und/oder Ethylacetat besteht.

9. Verfahren nach Anspruch 7 oder 8, wobei die Lösung in Stufe (b) bis zu 8h lang stehen gelassen wird.

10. Oral einnehmbares Produkt mit einem eine Masse nach einem der Ansprüche 1 bis 6 umfassenden Süßungsmittel, wobei das einnehmbare Produkt aus einem festen oder wässrigen Nahrungsmittel, einem flüssigen Getränk, einer Kaugummimasse, einem Mundwasser, einem Hustenbonbon, einem Atemfrischmacher oder einem Süßwaren- oder Zuckerwerkprodukt, z.B. Bonbons oder weichem Zukkerwerk, Schokolade oder Bisquit besteht.

11. Verfahren zur Herstellung einer oral einnehmbaren Arzneimittelzubereitung durch Einarbeiten eines Süßungsmittels, umfassend eine stabilisierte Masse nach einem der Ansprüche 1 bis 6, in eine Arzneimittelrezeptur.

Patentansprüche für folgende Vertragsstaat : ES

1. Verfahren zur Herstellung einer wärmestabilisierten Sucralosemasse, umfassend einen gemeinsam kristallisierten Komplex von Sucralose und mindestens 5 Gew. -% eines Cyclodextrins, durch
   (a) Auflösen der Sucralose und eines Cyclodextrins in einem geeignetem nicht-wässrigen Lösungsmittel;
   (b) ausreichend langes Stehenlassen der in Stufe (a) gebildeten Lösung zur vollständigen gemeinsamen Kristallisation der Sucralose und des Cyclodextrins;
   (c) Gewinnen und anschließendes Trocknen des kristallinen Reaktionsprodukts aus Stufe (b) und
   (d) Vermahlen des Materials aus Stufe (c) zu Teilchenform.

2. Verfahren nach Anspruch 1, wobei das Cyclodextrin aus α-Cyclodextrin, β-Cyclodextrin, γ-Cyclodextrin oder Mischungen derselben besteht.

3. Verfahren nach Anspruch 1 oder 2, wobei die Sucralose zumindest teilweise innerhalb des Cyclodextrins eingeschlossen ist.

4. Verfahren nach einem der vorhergehenden Ansprüche, wobei der Komplex mindestens 15 Gew. -% des Cyclodextrins enthält.

5. Verfahren nach einem der vorhergehenden Ansprüche, wobei das Material in Stufe (d) auf eine durchschnittliche Teilchengröße von etwa 10µm vermahlen wird.

6. Verfahren nach einem der vorhergehenden Ansprüche, wobei das nicht-wässrige Lösungsmittel aus Methanol und/oder Ethylacetat besteht.

7. Verfahren nach einem der vorhergehenden Ansprüche, wobei die Lösung in Stufe (b) bis zu 8h lang stehen gelassen wird.

8. Verfahren zur Zubereitung eines oral einnehmbaren Produkts durch Einarbeiten eines oral einnehmbaren Produkts mit einem Süßungsmittel, umfassend eine nach einem Verfahren gemäß einem der Ansprüche 1 bis 7 hergestellte Masse, in ein Produkt, wobei das einnehmbare Produkt aus einem festen oder wässrigen Nahrungsmittel, einem flüssigen Getränk, einer Kaugummimasse, einem Mundwasser, einem Hustenbonbon, einem Atemfrischmacher oder einem Süßwaren- oder Zuckerwerkprodukt, z.B. Bonbons oder weichem Zuckerwerk, Schokolade oder Bisquit besteht.

9. Verfahren zur Herstellung einer oral einnehmbaren Arzneimittelzubereitung durch Einarbeiten eines Süßungsmittels, umfassend eine nach einem Verfahren gemäß einem der Ansprüche 1 bis 7 hergestellte stabilisierte Masse, in eine Arzneimittelzubereitung.

Revendications

Revendications pour les Etats contractants suivants : BE, FR, DE, IT, NL, LI, SE, CH, GB

1. Une composition de sucralose thermiquement stabilisée comprenant un complexe de sucralose co-cristallisé et au moins 5% en poids d'une cyclodextrine.

2. Une composition selon la revendication 1, caractérisée en ce que la cyclodextrine est une α-cyclodextrine, β-cyclodextrine, γ-cyclodextrine ou leur mélange.

3. Une composition selon la revendication 1 ou la revendication 2, caractérisée en ce que le sucralose est au moins partiellement inclus dans la cyclodextrine.

4. Une composition selon la revendication 1, la revendication 2 ou la revendication 3, caractérisée en ce que le complexe contient au moins 15% en poids de cyclodextrine.

5. Une composition selon l'une quelconque des revendications précédentes, caractérisée en ce que le complexe est sous forme particulaire.

6. Une composition selon la revendication 5, caractérisée en ce que la dimension particulaire moyenne du complexe est approximativement de 10 µm.

7. Un procédé pour la préparation d'une composition de sucralose thermiquement stabilisée selon l'une quelconque des revendications 1 à 6, lequel procédé consiste à:
   a) dissoudre le sucralose et une cyclodextrine dans un solvant non aqueux approprié;
   b) maintenir la solution formée dans l'étape a) pendant une période de temps suffisante pour permettre l'entière co-cristallisation du sucralose et de la cyclodextrine;
   c) récupérer puis sécher le produit de réaction cristallin de l'étape b); et
   d) broyer le matériau de l'étape c) sous forme particulaire.

8. Un procédé selon la revendication 7, caractérisé en ce que le solvant non aqueux est du méthanol ou de l'éthyl-acétate, ou les deux.

9. Un procédé selon la revendication 7 ou 8, caractérisé en ce que la solution est maintenue dans l'étape b) jusqu'à 8 heures.

10. Un produit ingérable par voie orale contenant un édulcorant, caractérisé en ce que l'édulcorant comprend une composition selon l'une quelconque des revendications 1 à 6, dans laquelle le produit ingérable est un aliment solide ou aqueux; une boisson liquide; une composition de gomme à mâcher; une solution de lavage buccal; un adoucissant pour la toux; un rafraîchissant d'haleine; ou un produit de confiserie tel qu'un bonbon dur ou mou, un chocolat ou un biscuit.

11. Une préparation pharmaceutique ingérable par voie orale contenant un adoucissant qui comprend une composition selon l'une quelconque des revendications 1 à 6.

Revendications pour l'Etat contractant suivant : GR

1. Une composition de sucralose stabilisée thermiquement comprenant un complexe de sucralose co-cristallisé et au moins 5% en poids d'une cyclodextrine.

2. Une composition selon la revendication 1, caractérisée en ce que la cyclodextrine est une α-cyclodextrine, β-cyclodextrine, γ-cyclodextrine ou leur mélange.

3. Une composition selon la revendication 1 ou la revendication 2, caractérisée en ce que le sucralose est au moins partiellement inclus dans la cyclodextrine.

4. Une composition selon la revendication 1, 2 ou 3, caractérisée en ce que le complexe contient au moins 15% en poids de cyclodextrine.

5. Une composition selon l'une quelconque des revendications précédentes, caractérisée en ce que le complexe est sous forme particulaire.

6. Une composition selon la revendication 5, caractérisée en ce que la taille particulaire moyenne dans le complexe est approximativement de 10 μm.

7. Un procédé de préparation d'une composition de sucralose stabilisée thermiquement selon l'une quelconque des revendications 1 à 6, lequel procédé consiste à:
   a) dissoudre le sucralose et une cyclodextrine dans un solvant non aqueux approprié;
   b) maintenir la solution formée dans l'étape a) pour une période de temps suffisante à permettre la co-cristallisation complète du sucralose et de la cyclodextrine;
   c) récupérer puis sécher le produit de réaction cristallin de l'étape b); et
   d) broyer le matériau de l'étape c) en forme particulaire.

8. Un procédé selon la revendication 7, caractérisé en ce que le solvant non aqueux est du méthanol ou de l'éthyl-acétate, ou les deux.

9. Un procédé selon la revendication 7 ou la revendication 8, caractérisé en ce que la solution est maintenue dans l'étape b) jusqu'à 8 heures.

10. Un produit ingérable par voie orale contenant un édulcorant, caractérisé en ce que l'édulcorant comprend une composition selon l'une quelconque des revendications 1 à 6, dans laquelle le produit ingérable est un aliment aqueux ou solide; une boisson liquide; une composition de gomme à mâcher; une solution de lavage buccal; un adoucissant pour la toux; un rafraîchissant d'haleine; ou un produit de confiserie tel qu'un bonbon dur ou mou, un chocolat ou un biscuit.

11. Un procédé de préparation d'une composition pharmaceutique ingérable par voie orale qui comprend l'incorporation dans une préparation pharmaceutique d'un édulcorant comprenant une composition stabilisée selon l'une quelconque des revendications 1 à 6.

Revendications pour l'Etat contractant suivant : ES

1. Un procédé de préparation d'une composition de sucralose stabilisée thermiquement comprenant un complexe de sucralose co-cristallisé et au moins 5% en poids d'une cyclodextrine, lequel procédé comprend les étapes consistant à:
   a) dissoudre le sucralose et la cyclodextrine dans un solvant non aqueux approprié; et
   b) maintenir la solution formée au cours de l'étape a) pendant une période de temps suffisante à permettre à la co-cristallisation du sucralose et de la cyclodextrine de prendre place;
   c) récupérer puis sécher le produit de réaction cristallin de l'étape b); et
   d) broyer le matériau de l'étape c) sous forme particulaire.

2. Un procédé selon la revendication 1, caractérisé en ce que la cyclodextrine est une α-cyclodextrine, β-cyclodextrine, γ-cyclodextrine ou leur mélange.

3. Un procédé selon la revendication 1 ou la revendication 2, caractérisé en ce que le sucralose est au moins partiellement inclus dans la cyclodextrine.

4. Un procédé selon l'une quelconque des revendications précédentes, caractérisé en ce que le complexe contient au moins 15% en poids de cyclodextrine.

5. Un procédé selon l'une quelconque des revendications précédentes, caractérisée en ce que au cours de l'étape (d), le matériau est broyé en une dimension particulaire moyenne d'approximativement 10 µm.

6. Un procédé selon l'une quelconque des revendications précédentes, caractérisé en ce que le solvant non aqueux est du méthanol ou de l'éthylacétate ou les deux.

7. Un procédé selon l'une quelconque des revendications précédentes, caractérisé en ce que la solution est maintenue au cours de l'étape (b) pendant jusqu'à 8 heures.

8. Un procédé de préparation d'un produit ingérable par voie orale, qui comprend l'incorporation dans un produit ingérable par voie orale contenant un édulcorant, caractérisé en ce que l'édulcorant comprend une composition préparée par un procédé selon l'une quelconque des revendications 1 à 7, dans laquelle le produit ingérable est un aliment solide ou aqueux; une boisson liquide; une composition de gomme à mâcher; une solution de lavage buccal; un adoucissant pour la toux; un rafraîchissant d'haleine; ou un produit de confiserie tel qu'un bonbon dur ou mou, du chocolat ou du biscuit.

9. Un procédé de préparation d'une composition pharmaceutique ingérable par voie orale qui comprend l'incorporation dans une préparation pharmaceutique d'un édulcorant comprenant une composition stabilisée préparée par un procédé selon l'une quelconque des revendications 1 à 7.

FIG. 1

SUCRALOSE/CYCLODEXTRIN CRYSTALLINE
MINS DELAYED DISCOLORATION VS. SUCRALOSE

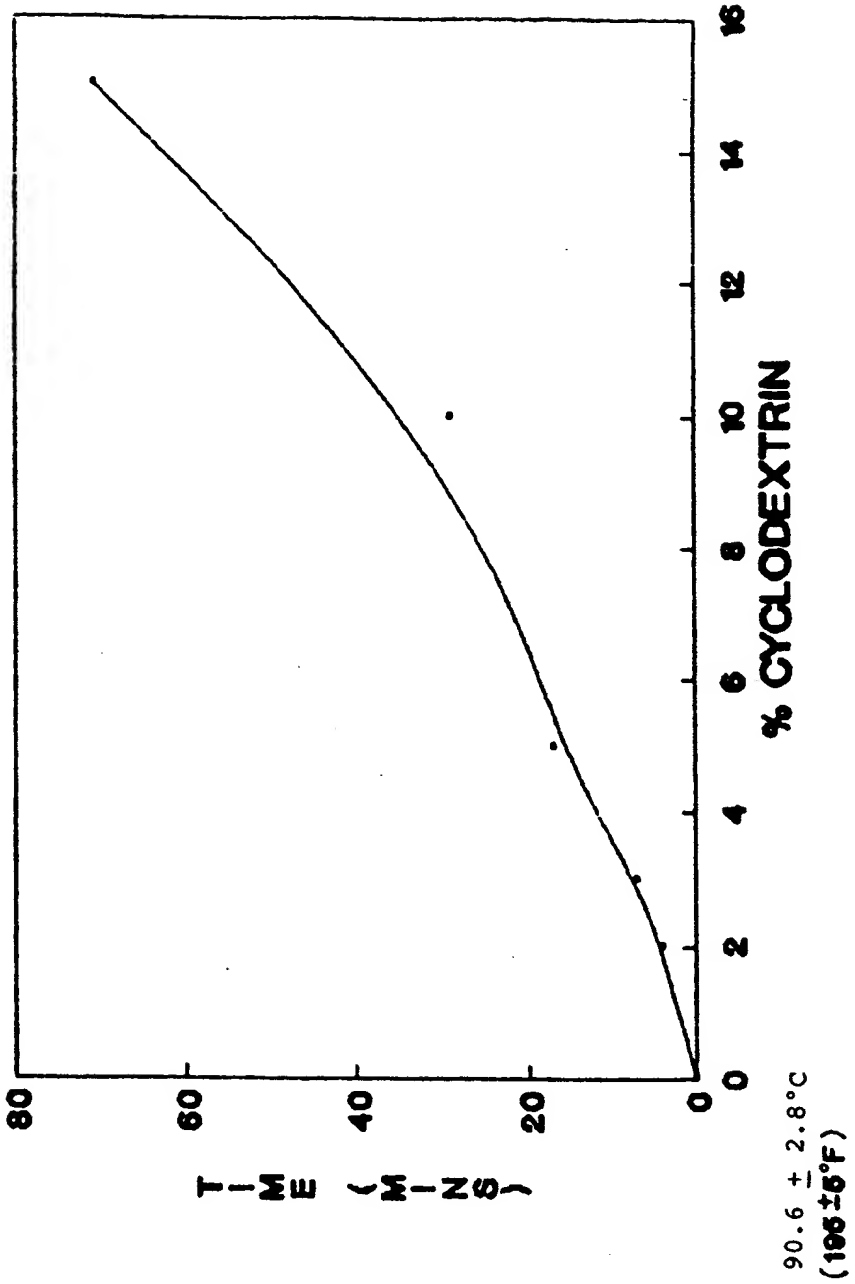


FIG.2 SWEETNESS INTENSITY IN CHEWING GUMS SUCRALOSE/B-CYCLODEXTRIN CO-CRYSTALLINE